mixture was poured into water and extracted with CH_2Cl_2. The layers were separated and the CH_2Cl_2 layer was dried over sodium sulfate. Chromatography (SiO_2; hexane–ether) gave a colorless oil: 31 mg (26%); NMR 1.90 (m, 2 H, CH_2), 2.33 (s, 4 H, $COCH_3$), 2.90 (m, 4 H, benzylic), 7.20 (s, 4 H, aromatic); IR 3525 (6 H), 1710 (c=O), 1600 (aromatic); mass spectrum, *m/e* 190 (M^+), 147 (M – $COCH_3$).

This compound was further identified by the preparation of its semicarbazone. 2-Acetyl-2-hydroxy-1,2,3,4-tetrahydronaphthalene (30 mg, 0.16 mmol) was added to a mixture of semicarbazide hydrochloride (150 mg, 1.05 mmol) and sodium acetate (50 mg) in a solution of 10 mL of EtOH and 5 mL of H_2O. after being heated for 1 min, the solution was then cooled to 0 °C. The semicarbazone crystallized out of solution. Recrystallization from acetic acid gave colorless crystals; mp 220–222 °C (lit.[6] mp 221–223 °C) (18 mg, 72%).

2,3-Bis(bromomethyl)-1,4-dimethoxybenzene. 2,3-Dimethyl-1,4-dimethoxy-benzene (166 mg, 1 mmol) and *N*-bromosuccinimide (445 mg, 2.5 mmol) were dissolved in dry carbon tetrachloride (150 mL) containing benzoyl peroxide (25 mg). The solution refluxed for 24 h. After the mixture cooled, the succinimide was filtered and the filtrate evaporated. The residue was washed with dilute base and then water and dried. Chromatography (SiO_2, C_6H_6) and recrystallization from petroleum ether gave colorless crystals: mp 147–149 °C (lit.[7] mp 149 °C) (264 mg, 81%); NMR 3.85 (s, 6 H, 2 OCH_3), 4.61 (s, 4 H, 2 CH_2Br), 6.70 (s, 2 H, aromatic).

2-Acetyl-2-hydroxy-5,8-dimethoxy-1,2,3,4-tetrahydronaphthalene. 2,3-Bis(bromomethyl)-1,4-dimethoxybenzene (160 mg, 0.5 mmol) was added portionwise to a stirred suspension of 3-(trimethylsiloxy)-3-buten-2-one (2.0 g), hydroquinone (10 mg), activated zinc dust (1.0 g), and 10 mL of dry DMF. After the mixture was stirred for 30 min, the zinc was filtered. The organic layer was then acidified with HOAc and heated to 45 °C for 2 h. The solution was poured into H_2O and filtered. The residued was chromatographed (SiO_2, C_6H_6). Recrystallization from petroleum ether gave colorless crystals: mp 96–97 °C (lit.[4b] mp 97 °C) (23 mg, 17%); NMR 1.90 (m, 2 H, CH_2), 2.33 (s, 3 H, $COCH_3$), 2.90 (m, 5 H, benzylic and OH), 3.78 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 6.66 (s, 2 H, aromatic); IR 3525 (OH), 1705 (C=O), 1600 (aromatic); mass spectrum, *m/e* 250 (M^+), 207 (M – $COCH_3$).

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Registry No. 1, 42082-94-0; 2, 91-13-4; 3, 19164-83-1; 4, 76376-98-2; 5, 76376-99-3; 6, 76377-00-9; 7, 76377-01-0; 7 semicarbazone, 76377-02-1; 8, 71366-25-1; cyclopentadiene, 542-92-7; diphenylisobenzofuran, 5471-63-6; tetraphenylcyclopentadienone, 479-33-4; 2,3-dimethyl-1,4-dimethoxybenzene, 39021-83-5; anthracene, 120-12-7; 9,10-dimethylanthracene, 781-43-1.

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Ortho Ester Claisen Rearrangements Using Trimethyl Methoxyorthoacetate

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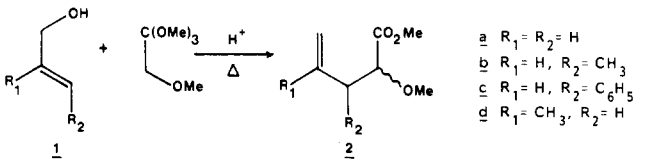
During the past 10 years the Claisen rearrangement has been developed into a very general and powerful synthetic tool.[1] In particular, enolate Claisen methods[2] and ortho ester/ketal exchange procedures[3] have provided the synthetic chemist with convenient new methods for exploiting this historically important pathway to γ,δ-unsaturated carbonyl compounds.

Scheme I



The generality of these methods has typically been demonstrated by substituting the basic allyl vinyl ether framework with alkyl or aryl groups. Only in a few cases has a heteroatom been included as a substituent.[2,4-8] Ireland[2,8] and Still[5] have previously demonstrated that heteroatom substitution is compatible with the enolate Claisen reaction, which proceeds under basic conditions. Recent efforts in our laboratory have centered around the use of an α-methoxy ortho ester in the ortho ester Claisen rearrangement, a process that occurs under acidic conditions.

Trimethyl methoxyorthoacetate[9] participates as the ortho ester partner in the Claisen rearrangement (Scheme I), producing α-methoxy γ,δ-unsaturated methyl esters in fair yields (20–55%). The allylic alcohol 1 was heated (100–125 °C) with 2 equiv of trimethyl methoxyorthoacetate in the presence of a weak acid for 18 h at ambient pressure (method A) or in a sealed tube (method B). Shorter or longer reaction times did not appear to be beneficial. Gas chromatography indicated that the crude reaction mixture usually contained >10 components, with the desired product predominating. Subsequent chromatography on silica gel afforded the α-methoxy esters **2**.

The α-methoxy esters (**2**) were characterized by spectroscopic (IR, ^1H NMR, mass spectra) and chromatographic (TLC, VPC) methods. In cases where diastereomeric mixtures were expected (**2b**, **2c**), careful ^1H NMR analysis confirmed the presence of a ca. 1:1 mixture of the threo and erythro isomers. In particular, the methoxy and carbomethoxy protons in **2c** exhibited different chemical shifts (Δ = 3.0 Hz), while the methyl doublets in **2b** showed a somewhat smaller chemical shift difference (Δ = 1.2 Hz). We attribute the larger observed chemical shift difference in **2c** to the presence of the strong anisotropic effects of the aromatic ring. These diastereomeric mixtures proved inseparable by chromatography (TLC, VPC).

A reaction attempted between trimethyl methoxyorthoacetate and cyclohex-2-en-1-ol afforded no material that was consistent with the anticipated α-methoxy ester. Thus, the competing elimination reactions inherent in the ortho ester modification of the Claisen rearrangement render this method ineffective as well.[1b]

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Although the α-methoxy esters proved to be reasonably stable, they decomposed slowly during storage to complex mixtures. Column chromatography of the crude product mixture was unsuccessful on a few occasions and afforded little or no characterizable material. This leads us to believe that the isolated yields may be artificially low, owing to decomposition of the sensitive products on the silica gel.

These results demonstrate that the ortho ester Claisen rearrangement tolerates the presence of a heteroatomic substituent (OCH_3) directly on the allyl vinyl ether framework. While heteroatomic groups are present in the work of Johnson[4] (Cl) and Rauscher[6,7] (SePh, OCH_3), they are present in positions remote to the rearranging framework.

Experimental Section

Infrared spectra were determined on a Perkin-Elmer 137 sodium chloride spectrophotometer. ^1H NMR spectra were determined in $CDCl_3$, using a Varian EM 360L NMR spectrometer and were reported in parts per million relative to tetramethylsilane. Mass spectrometry was performed on a Finnigan 3200 GC/MS system. Vapor-phase chromatograms were obtained on a Varian Aerograph Series 1200 fitted with a $^1/_8$ in. × 12 ft 5% SE-30 on Gas Chrom Z column and a flame-ionization detector. Thin-layer chromatography was performed on precoated TLC sheets, using silica gel as supplied by E. Merck (no. 5575) and a solvent mixture of 7:2:1 of hexane–dichloromethane–acetone. Catalog 7734 silica gel 60 (particle size 0.063–0.2000 mm), available from Merck, was used as a support in column chromatography.

General Procedures for Ortho Ester Claisen Rearrangement. Method A. This procedure is a modification of Johnson's.[3] The allylic alcohol (5 mmol) and propionic acid (2 drops) were dissolved in trimethyl methoxyorthoacetate[9] (10 mmol). The solution was heated to 100–125 °C (depending on the boiling point of the alcohol) in a short-path distillation apparatus for 18 h, and methanol was collected in the receiving flask as it was formed. After cooling, the reaction mixture was diluted with ether and washed with saturated $NaHCO_3$, water, and brine. After the solution was dried ($MgSO_4$) and concentrated under reduced pressure, VPC analysis indicated the presence of the desired ester, trimethyl methoxyorthoacetate, the allylic alcohol, and 5–10 minor unidentified components. The esters were purified by column chromatography on silica gel, using a step gradient (0%, 1%, 2%, 5%, 10%, 20%, total volume = 600 mL) of ether/hexane mixtures as eluants. The remaining ortho ester is eluted in the early fractions (1–10, 0–1% Et_2O/hexane), the product is eluted in the middle fractions (20–40, 5–10% Et_2O/hexane), and the residual allylic alcohol generally eluted in the later fractions (>40, 20% Et_2O/hexane).

Method B. The allylic alcohol (5 mmol) and propionic acid (2 drops) were dissolved in trimethyl methoxyorthoacetate (10 mmol) and the solution was sealed in a 25-mL pressure reaction bottle (Cal-Glass, no. LG3921). After being heated at 125 °C for 18 h, the reaction mixture was worked up and purified as described in method A.

Methyl 2-Methoxy-4-pentenoate (2a). Methyl 2-methoxy-4-pentenoate was prepared from allyl alcohol in yields of 28% (method A) and 25% (method B). The desired product was eluted in fractions 43–50 (10 mL each, 10% ether/hexane): IR (film) ν_{max} 2900, 1730, 1640, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.50 (t, 2 H, J = 6.0 Hz), 3.38 (s, 3 H), 3.73 (s, 3 H), 3.85 (t, 1 H, J = 6.0 Hz), 5.00–5.20 (m, 2 H), 5.50–6.17 (m, 1 H); TLC R_f 0.51; VPC (100 °C) t_R 2.45 min; mass spectrum, m/e 144, 112 ($M^+ - CH_3OH$), 103, 85 (100).

Methyl 2-Methoxy-3-methyl-4-pentenoate (2b). Methyl 2-methoxy-3-methyl-4-pentenoate was prepared from crotyl alcohol in yields of 25% (method A) and 20% (method B). The desired product was eluted in fractions 28–36 (12 mL each, 5% ether/hexane): IR (film) ν_{max} 2900, 1730, 1630, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06/1.08 (d/d, 3 H, J = 7.0 Hz, 1:1 mixture of diastereomers), 2.57 (m, 1 H), 3.37 (s, 3 H), 3.67 (d, 1 H, J = 7.0 Hz), 3.73 (s, 3 H), 4.83–5.23 (m, 2 H), 5.40–6.00 (m, 1 H); TLC R_f 0.56; VPC (100 °C) t_R 3.78 min; mass spectrum, m/e 158, 126 ($M^+ - CH_3OH$), 104, 103, 99 (100).

Methyl 2-Methoxy-3-phenyl-4-pentenoate (2c). Methyl 2-methoxy-3-phenyl-4-pentenoate was prepared from cinnamyl alcohol in a yield of 55% (method A). The desired product was eluted in fractions 26–45 (12 mL each, 10% ether/hexane): IR (film) ν_{max} 2900, 1730, 1630, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.30/3.50 (s/s, 3 H, 1:1 mixture of diastereomers), 3.60/3.65 (s/s, 3 H, 1:1 mixture of diastereomers), 3.67–4.17 (m, 2 H), 4.83–5.33 (m, 2 H), 5.77–6.50 (m, 1 H), 7.27 (s, 5 H); TLC R_f 0.40; VPC (170 °C) t_R 3.00 min; mass spectrum, m/e (no M^+ observed), 188 ($M^+ - CH_3OH$), 161, 117 (100).

Methyl 2-Methoxy-4-methyl-4-pentenoate (2d). Methyl 2-methoxy-4-methyl-4-pentenoate was prepared from methallyl alcohol in a yield of 23% (method B). The desired product was eluted in fractions 41–46 (10 mL each, 10% ether/hexane): IR (film) ν_{max} 2900, 1725, 1630, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77 (s, 3 H), 2.43 (d, 2 H, J = 7.0 Hz), 3.37 (s, 3 H), 3.73 (s, 3 H), 3.93 (t, 1 H, J = 7.0 Hz), 4.80 (m, 2 H); TLC R_f 0.69; VPC (100 °C) t_R 4.25 min; mass spectrum, m/e 158, 126 ($M^+ - CH_3OH$), 103, 99 (100).

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Registry No. 1a, 107-18-6; **1b**, 6117-91-5; **1c**, 104-54-1; **1d**, 513-42-8; **2a**, 54020-52-9; **2b** (isomer 1), 76376-93-7; **2b** (isomer 2), 76376-94-8; **2c** (isomer 1), 76376-95-9; **2c** (isomer 2), 76376-96-0; **2d**, 76376-97-1; trimethyl methoxyorthoacetate, 34359-77-8.

Novel Synthetic Route to Angularly Functionalized Hydrofluorene Derivatives by a Regio- and Stereospecific Metalation–Carbonation Reaction

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A selective metalation–carbonation reaction has been used for the introduction of C-1 and C-9 carboxyl groups into hydrofluorene[1,2] and gibbane[3] systems (corresponding to the C-4 and C-6 positions in gibberellane), leading to a few useful gibberellin synthons. As shown by House,[1] the lithiation–carbonation of the tetrahydrofluorene **1a** produces mostly the benzylic carboxylic acid **2a** along with only a minor amount of its angular regioisomer **3a** (Scheme I) The acid **1b**,[1,2] on the other hand, results in an ~1:1 mixture of **2b** and **3b** under similar reaction conditions as depicted in Scheme I.

We report here a remarkable influence by a neighboring *gem*-carboxymethyl group in the tetrahydrofluorene sub-

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